

AMENDMENT OF THE DRAWINGS

Please substitute Figures 1-41 with the attached replacement drawings of Figures 1-41 (47 sheets).

REMARKS

Reconsideration of this application, as amended, is respectfully requested.

A. Status of the claims

Claims 433-437 and 439-446 are pending in this application.

B. Objection to the Drawings

In response to the objection to Figures 1-41, replacement Figures 1-41 (47 sheets) are enclosed. The replacement figures are formal versions of the original figures and no new matter is added. Withdrawal of the objection is respectfully requested.

C. Rejection under 35 U.S.C. section 102(e) or 103(a) in view of Yguerabide

Claims 433-437 and 439-446 stand rejected under 35 U.S.C. section 102(e) as being anticipated by, or in the alternative, under 35 USC section 103(a) as being obvious over Yguerabide (U.S. Patent No. 6,214,560) ("Yguerabide"). The Applicants respectfully traverse this rejection.

As a threshold matter, the Federal Circuit has stated that for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. Corning Glass Works v. Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983).

Likewise, the Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." In re Vaeck, 947 F.2d

488, 493, 20 U.S.P.Q.2d 1438, 1485 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). Contrary to the Examiner's position, the Applicants submit that Yguerabide does not teach or suggest what the Applicants have done.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using gold particulate labeled probes and that the recited surface density is obvious. Applicants respectfully traverse.

With respect to surface density, Yguerabide in col. 82, line 35, merely discusses surface density of the number of particles present in a spot on a substrate. However, a disclosure of particle density on a surface of a substrate is not a disclosure of oligonucleotide density on a surface of a particle. Col. 83 provides further discussion regarding particle size and particle binding to a surface. Cols. 77-80 relate to particles and their preparation. Col. 110 (Example 32) relates to a nucleic acid labeled particle but does not provide or suggest any particle surface density. Indeed, no particle surface density can be calculated from Yguerabide's disclosure since he does not provide any DNA concentrations that are necessary to calculate surface density. Thus, Yguerabide is completely silent with respect to any particle having oligonucleotides with a surface density of at least 10 picomoles/cm² as recited in claim 433. Yguerabide cannot be relied on to support a section 102(e) or 103(a) rejection of the present claims.

Furthermore, the Examiner alleged that the recitations "recognition oligonucleotides", "spacer portion" and "diluent oligonucleotide" are overly broad and would encompass any nucleotide sequence. Applicants respectfully traverse.

As described in the specification, "recognition oligonucleotides" refers to oligonucleotides which comprise a "sequence complementary to at least a portion of the sequence of a nucleic acid or oligonucleotide target." See page 22, lines 2-3.

Furthermore, "diluent oligonucleotides" may have any sequence which "does not interfere with the ability of the recognition oligonucleotides to be bound to the nanoparticles or to bind to their targets." See page 22, lines 4-6. As discussed in the specification, the use of diluent oligonucleotides in addition to recognition oligonucleotides provides a means of tailoring the conjugates to give a desired level of hybridization. The diluent and recognition oligonucleotides have been found to attach to the nanoparticles in about the same proportion as their ratio in the solution contacted with the nanoparticles to prepare the conjugates. Thus, the ratio of the diluent

to recognition oligonucleotides bound to the nanoparticles can be controlled so that the conjugates will participate in a desired number of hybridization events. While the diluent oligonucleotides may have any sequence, the sequence is one which does not interfere with the ability of the recognition oligonucleotides to be bound to the nanoparticles or to bind to a nucleic acid or oligonucleotide target. For instance, the diluent oligonucleotides should not have a sequence complementary to that of the recognition oligonucleotides or to that of the nucleic acid or oligonucleotide target of the recognition oligonucleotides. The diluent oligonucleotides are also preferably of a length shorter than that of the recognition oligonucleotides so that the recognition oligonucleotides can bind to their nucleic acid or oligonucleotide targets. If the recognition oligonucleotides comprise spacer portions, the diluent oligonucleotides are, most preferably, about the same length as the spacer portions. In this manner, the diluent oligonucleotides do not interfere with the ability of the recognition portions of the recognition oligonucleotides to hybridize with nucleic acid or oligonucleotide targets. If desired, the diluent oligonucleotides have the same sequence as the sequence of the spacer portions of the recognition oligonucleotides. See the specification at page 80, lines 8-27.

The “spacer portions” of the recognition oligonucleotides allows for binding of the recognition oligonucleotides onto nanoparticles and for spacing away of the recognition portion of the recognition oligonucleotides away from the nanoparticle surface so that the recognition portion is more accessible for hybridization with a target. See page 22, lines 13-16. As discussed in the specification, the spacer portion may have any sequence which “does not interfere with the ability of the recognition oligonucleotides to become bound to the nanoparticles or to a nucleic acid or oligonucleotide target.” See page 79, line 17 to page 80, line 7.

In light of the teachings in the specification, a person of ordinary skill in the art would appreciate that recognition oligonucleotides, diluent oligonucleotides and spacer portions are limited in scope. Furthermore, there is no discussion or suggestion anywhere in Yguerabide of any nanoparticle comprising recognition and diluent oligonucleotides and spacer portions of recognition oligonucleotides as presently claimed.

In summary, the present claims recite limitations that are neither taught, made obvious, or suggested by the cited reference. Thus, the Applicant respectfully submits that Yguerabide

cannot be applied to support section 102(e) and/or section 103(a) rejections of the claims. Withdrawal of these rejections is in order and is respectfully requested.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Respectfully submitted,



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